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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,536	07/29/2003	Paula M. McCready	IL-11030	3210

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EXAMINER	
BAUSCH, SARAE L	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/630,536	MCCREADY ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-15* is/are pending in the application.

4a) Of the above claim(s) *4-7, 9-10, and 14-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8, 11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 4-15 are pending in the instant application. Claim 1-3 and 16-17 have been canceled. Claims 4-7 are withdrawn. Claims 9-10 and 14-15 are withdrawn as being drawn to a non-elected invention, see page 3 of the office action mailed 08/07/2006. This action is written in response to applicant's correspondence submitted 02/12/2007. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, as necessitated by amendment, or are reiterated from the previous office action. Any rejections not reiterated in this action have been withdrawn as necessitated by applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is Non-Final.**

2. Currently, claims 8, 11-13 and the combination of SEQ ID No. 4 and 8 and the set of oligonucleotides SEQ ID No. 1-3 and 5-7 are under examination on the merits.

Withdrawn Rejections

3. The rejections of claims 8 and 11-13, under 35 U.S.C. 112(1) made in section 7 and 8 of the previous office action, is withdrawn in view of the amendment to the claims.

4. The rejections of claims 8 and 11-13, under 35 U.S.C. 102(b), made in section 10 of the previous office action, is withdrawn in view of the amendment to the claims.

Specification

5. The abstract of the disclosure is objected to because the abstract begins with "described herein". Correction is required. See MPEP § 608.01(b).

New Grounds of Rejection

Claim Rejections - 35 USC § 112- Second Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 8 and 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a). Claim 8 and 11 are indefinite for the recitation of "full length complement" in claim 8 and claim 11. The metes and bounds of the claim with the recitation of "full-length complement" is unclear, as it is unclear if the complement is of the entire sequence of SEQ ID No. 4 or 8.

(b). Claim 8 recites the limitation of "the second polynucleotide" in lines 3-4 of the claim. There is insufficient antecedent basis for this limitation in the claim. The claim recites a "second isolated polynucleotide" but does not recite any second polynucleotide. Therefore, claim 8 is indefinite because it is unclear which second polynucleotide is present in the composition.

(c). Claims 11-13 depend from claim 8 and are indefinite for the reasons applied to claim 8.

Claim Rejections - 35 USC § 112- New Matter

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 8 and 11-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly amended claim(s) contain subject matter that changes the scope of the claim and is not supported in the specification and raises issues of new matter.

Amended claim 8 with the recitation "the first isolated polynucleotide consists of SEQ ID No. 4" and the recitation of "the second polynucleotides that consists of SEQ ID No. 8" changes the scope of the claim and a compositions consisting of SEQ ID No. 4 and 8 is not supported in the specification and raises the issue of new matter. The specification does not teach a composition that comprises two isolated polynucleotides that consists of SEQ ID No. 4 and 8. The originally filed claims recite a composition comprising "an" amplicons (see claim 1) and the specification teaches that nucleotide sequence are identified in SEQ ID No. 4, 8, 12, 16, and 20 (see paragraph 6). However, the specification does not teach the amplicons that consist of SEQ

ID no. 4 and 8 in a composition together. The specification teaches that the typical assay determines the presence of SEQ ID No. 4 and 8 using the sequence specific primers and the hybridization probes (see paragraph 16). The specification discloses that a series of forward and reverse primers, hybridization probe and polymerase reagents specific to the first amplicons are needed and that a series of forward and reverse primers, hybridization probe and polymerase reagents specific to the second amplicons are needed (see page 9, materials needed). However, the specification does not disclose a composition that consists of SEQ ID no. 4 and 8, nor does the specification teach a PCR reaction that would result in a composition that would comprise two isolated polynucleotides that consist of SEQ ID No. 4 and 8. The specification does teach a sample that comprises two polynucleotides that comprise SEQ ID No. 4 and 8, the sample provided in PCR reaction (see paragraph 19), however it does not teach a sample or any composition that consists of SEQ ID No. 4 and 8.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 8 and 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. (J. Bacteriol. 1998, vol. 180, pages 5192-5202) in view of GenBank Accession number AF053947 and Hogan et al. (US Patent 5541308).

Hu et al. analysis of the pMT1 virulence associated plasmid of Yersinia pestis. The plasmid, pMT1 compromises nucleotides 85237-85136 which are identical to SEQ ID No. 4 and nucleotides 13354-13500, which are identical to SEQ ID No. 8 (alignment provided on 08/07/2006). Hu et al. teaches that SEQ ID No. 4 is part of the gene for murine toxin (see table 3). Hu et al. teach pMT1 is the largest plasmid and contains the important gene of plague murine toxin and also contains atypical base composition regions that are pathogenicity islands that participate in pathogenicity and contribute to difference in host specificity, tissue tropism and disease manifestation (see pg. 5199, 2nd column, last paragraph). Hu et al. teach that the entire nucleotide sequence enables the global study of the gene complement encoded by them and allow for insight into the interplay of virulence factors that are unique to Y. pestis. Hu et al. does not teach a composition comprising a first isolated polynucleotides consisting of SEQ ID No. 4 and a second isolated polynucleotide consisting of SEQ ID No. 8. Hu et al. does not teach fragments of isolated polynucleotides that are 18-33 nucleotides in length nor does Hu et al. teach SEQ ID No. 1-3 and 5-7.

GenBank accession number AF053947 teaches the entire genomic sequence of plasmid, pMT1 of Y. pestis. The genomic sequence of pMT1 comprises nucleotides 85237-85136

(identical to SEQ ID No. 4) and nucleotides 13354-13500 (identical to SEQ ID No. 8). Furthermore, the sequence AF053947 comprises SEQ ID No. 1-3 and 5-7.

Hogan et al. teaches the use of specific primers and probes to amplify the 16S region of bacteria. Hogan et al. provides guidance for the selection of probes.

> "Once the variable regions are identified, the sequences are aligned to reveal areas of maximum homology or 'match'. At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We have identified the following useful guidelines for designing probes with the desired characteristics.
> Fist, probes should be positioned so as to minimize the stability of the probe: nontarget nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarily to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe: target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G: C base pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10 °C higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structure inhibitory to hybridization are less preferred. Finally probes with extensive self complementarity should be avoided." (See Column 6 lines 66-67 and Column 7 lines 1-29).

Hogan et al. teaches, "while oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 15 and about 50 bases in length" (see Column 10, lines 13-15). Therefore Hogan et al. teaches taking a sequence and fragmenting the sequence into smaller oligonucleotides to be used as probes. Hogan et al. teaches that these probes are preferable to be between about 15 and about 50 bases in length. Though, Hogan et al. does not specifically teach the SEQ ID Nos 1-3 and 5-7, he does suggest the fragmentation of a larger fragment (i.e. the GenBank Accession Number AF053947) into smaller oligonucleotide probes.

Therefore, the ordinary artisan would have been motivated to select any number of oligonucleotide fragments from Accession Number AF05397 and the sequence provided by Hu et al. to include SEQ ID Nos 1, 2, 3, 5, 6, and 7 which are fragments of SEQ ID No. 4 and 8 that

are contained by Accession Number AF05397. Furthermore, Hu et al. teach pMT1, AF05397 is the largest plasmid and contains the important gene of plague murine toxin and also contains atypical base composition regions that are pathogenicity islands that participate in pathogenicity and contribute to difference in host specificity, tissue tropism and disease manifestation and teaches that the entire nucleotide sequence enables the global study of the gene complement encoded by them and allow for insight into the interplay of virulence factors that are unique to Y. pestis. Therefore the ordinary artisan would have been motivated to isolate and select any fragment within the pMT1 plasmid to detect Y. pestis, including the amplicons of SEQ ID No. 4 and 8. The art of designing probes (oligonucleotides) and resulting amplicons at the time the invention was made was very well described in the art. The art uses alignment programs to align sequences of interest and then uses algorithms to select and test probes and primers for their desired function of either detecting or distinguishing particular organisms. Designing probes and regions of interest that result in amplicons that are equivalents to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan et al. Moreover there are many Internet web sites that provide free downloadable software to aid in the selection of probes drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes, primers, and resulting amplicons. The claimed probes, primers, and amplicons are prima facie obvious over the cited references in the absence of secondary considerations, given the extensive teachings in the art. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use an amplified sequence of Yersinia as taught by

Hu et al, GenBank access No. AF05397 and design constraints of probes taught by Hogan et al. to obtain equivalent alternative probes, primers, and amplicons of the claimed invention. The ordinary artisan would be motivated to have designed and test new probes to obtain additional oligonucleotides that function to detect Yersinia and identify oligonucleotides with improved properties.

Conclusion

13. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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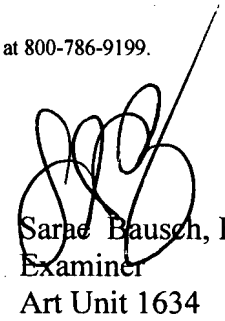

Sarae Bausch, PhD
Examiner
Art Unit 1634